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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/719,734	11/21/2003	Solomon S. Steiner	PDT120121DIVCON	3538

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ALSTRUM ACEVEDO, JAMES HENRY	
ART UNIT	**PAPER NUMBER**
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/719,734	STEINER ET AL.	
	Examiner	Art Unit	
	James H. Alstrum-Acevedo	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33 and 35-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33 and 35-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/25/07; 8/29/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 33 and 35--42 are pending. Applicants previously cancelled claims 1-32 and 34. Applicants have amended claims 33 and 35-38. Receipt and consideration of Applicants' new IDS (submitted 9/26/06), amended claim set, and remarks/arguments submitted on November 14, 2006 are acknowledged.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/9/07 has been entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 41 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 41 is indefinite because it claims a method of claim 40 wherein the composition is administered concurrently with, or "less than about 20 minutes prior" The phrase "less than about" is indefinite, because it simultaneously claims two different ranges. An ordinary skilled

artisan would be unable to ascertain whether the required amount of time between administration of the composition and eating a meal is less than 20 minutes or about 20 minutes. Appropriate correction is required.

The remaining claims are rejected as depending from a rejected claim.

Art Rejections of Record

All outstanding art (i.e. under both 35 U.S.C. § 102(b) and 103(a)) and both provisional and non-provisional obviousness-type double patenting rejections maintained in the office action mailed February 7, 2007 are maintained herein for the reasons already of record.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 33 and 36 under 35 U.S.C. 102(b) as being anticipated by Feldstein et al. (U.S. Patent No. 5,352,461) **is maintained** for the reasons of record set forth on page 3 of the office action mailed on May 17, 2006.

The rejection of claims 33, 35, and 37-38 under 35 U.S.C. 102(b) as being anticipated by Steiner et al. (U.S. Patent No. 5,503,852) **is maintained** for the reasons of record set forth on page 3-4 of the office action mailed on May 17, 2006.

Response to Arguments

Applicant's arguments filed 10/9/07 have been fully considered but they are not persuasive. Applicants' traversal of the instant rejection is based on their assertion that (1) the comparative data presented in declaration format demonstrates that the compositions and methods disclosed by Feldstein and Steiner allegedly do not anticipate the compositions utilized in the instantly claimed method, because the Feldstein or Steiner diketopiperazine microparticles are different than those claimed by Applicants; (2) Feldstein and Steiner allegedly do not anticipate the claimed methods because Feldstein and Steiner do not describe the disclosed diketopiperazine microparticles as comprising "complexed insulin"; and (3) that the insulin diketopiperazine microparticles made by complexation exhibited greater stability than the insulin-complexed diketopiperazine microparticles disclosed by either Feldstein or Steiner.

The Examiner respectfully disagrees with Applicants' traversal arguments. The term "complexed" is broad and is not defined by Applicants' specification to have a particular meaning. Applicants indicated that the method utilized to prepare the complexed insulin diketopiperazine microparticles that exhibited the greater stability in the data presented in the declaration is disclosed on page 16, lines 3-7 of the instant specification. It is noted that the procedure for making Applicants' "complexed insulin diketopiperazine microparticles" never recites a complexation step. Instead Applicants cited excerpt from their specification indicates that the insulin diketopiperazine microparticles of the claimed method are prepared by (1) preparing and providing a suspension of diketopiperazine microparticles; (2) addition of an aqueous solution of active agent; and (3) lyophilization or freeze drying of the resulting suspension yields diketopiperazine particles having a coating of active agent. Coincidentally, it

is noted that Applicants on page 16 indicate that the diketopiperazine microparticles have a higher affinity for insulin than zinc and Applicants imply that the diketopiperazine microparticles are complexing agents (see instant specification, pg. 16, lines 13-14 and 20). It is also noted that Applicants indicate that the ***term "entrapped" with reference to an active agent in/with a diketopiperazine includes coating of the active agent onto diketopiperazine microparticles***. Both Steiner and Feldstein indicate that their invented diketopiperazine microparticles comprise encapsulated insulin (see Steiner Example 3 or Feldstein Example 2). Both the Steiner and Feldstein diketopiperazine microparticles are prepared by precipitation of the microparticles upon combination of a solution of diketopiperazine with a solution of insulin. It is inevitable that the Steiner and Feldstein diketopiperazine microparticles both contain encapsulated insulin and insulin coating the surfaces of said diketopiperazine microparticles. Thus, given Applicants' disclosure, the fact that the Steiner and Feldstein diketopiperazine microparticles comprise the same components as Applicants diketopiperazine microparticles, it necessarily follows that the Steiner and Feldstein diketopiperazine microparticles inherently comprise complexed insulin. Regarding the property of releasing dimeric or monomeric insulin, this is a property of the diketopiperazine microparticles and a property cannot be separated from a composition. Finally, it is noted that Applicants' claims are not drawn to the different diketopiperazine microparticles associated with the "complexed diketopiperazine microparticles" in Applicants' declaration, because the particles exhibiting a greater stability were made by a specific methodology which does not include the explicit step of "complexing" insulin and diketopiperazine microparticles. In conclusion, Applicants claims are not patentably distinguishable from the disclosures and diketopiperazine microparticles invented by both Steiner and Feldstein.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejection of claims 33 and 35-39 under 35 U.S.C. 103(a) as being unpatentable over Milstein (U.S. Patent No. 5,976,569) ("Milstein") **is maintained** for the reasons of record set forth on page 5-7 of the office action mailed on May 17, 2006.

Response to Arguments

Applicants' arguments filed 10/9/07 have been fully considered but they are not persuasive. Applicants' traversal of the instant rejection is based on their assertion that (1) the teachings of Milstein are allegedly deficient because these teachings do not state that the diketopiperazines matrix is complexed with insulin or that the insulin is monomeric or dimeric; (2) one allegedly cannot extrapolate from the co-precipitation methods to a method that results in complexation between insulin and diketopiperazine microparticles.

This is found unpersuasive. Similarly, as was explained above in the instant office action, the formation of a complex between a diketopiperazine and insulin is obviously a process that would occur as a consequence of the close physical association between insulin and the diketopiperazine. The arguments submitted in rebuttal to Applicants' traversal arguments above are incorporated herein by reference. Specifically, Applicants' declaration data is not commensurate in scope with Applicants' claimed invention, because the term "complexed" does not indicate the method used to prepare that diketopiperazine microparticles exhibiting the greater stability in Applicants' declaration data. Regarding the delivery of monomeric or dimeric insulin, it is obvious that this would be a consequence of administering Milstein's microparticles, because even if the insulin were hexameric, it would eventually form monomeric and dimeric insulin, as Applicants' have admitted on the record (see page 2, line 23 through page 3, line 2). Therefore,

administration of Milstein's microparticles would obviously achieve the result of administering monomeric or dimeric insulin. For these reasons, the Examiner concludes that a person of ordinary skill in the art at the time of the instant invention would have found the cited claims *prima facie* obvious over the teachings of Milstein. The instant rejection remains proper.

The rejection of claims 40-42 under 35 U.S.C. 103(a) as being unpatentable over Milstein et al. (U.S. Patent No. 5,976,569) and further in view of Edelman, S.V. **is maintained** for the reasons of record set forth on page 7-9 of the office action mailed on May 17, 2006.

Response to Arguments

Applicant's arguments filed 10/9/07 have been fully considered but they are not persuasive. Applicants' traversal arguments of the instant rejection are the same as those submitted to contest the rejection of claims 33 and 35-39 as being unpatentable over Milstein and that the combination with Edelman does not cure the deficiencies of Milstein. The Examiner respectfully disagrees. The Examiner's position regarding these arguments remains the same and is reapplied here in full. For the aforementioned reasons set forth above in the instant office action, the Examiner concludes that a person of ordinary skill in the art at the time of the instant invention would have found claims 40-42 *prima facie* obvious over the combined teachings of Milstein and Edelman. The instant rejection remains proper.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The rejection on the ground of nonstatutory obviousness-type double patenting of claims 33 and 35-39 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4-7, and 10-14 of U.S. Patent No. 6,071,497 (USPN '497) **is maintained** for the reasons of record set forth on page 10 of the office action mailed on May 17, 2006.

Response to Arguments

Applicant's arguments filed 10/9/07 have been fully considered but they are not persuasive. Applicants' traversal is based on their assertion that the claims of USPN '497 do not define microparticles wherein insulin is complexed with microparticles of a diketopiperazine.

The Examiner respectfully disagrees. Applicants' arguments are the same as those discussed previously in the instant office action and the Examiner's position is the same as applied to the instant rejection. The microparticles of USPN '497 would obviously form complexes with insulin, especially since the same microparticles are being used. It is noted that the chemical structure and description thereof used to define the diketopiperazines in the original specifications of USPN '497 (i.e. col. 4, lines 1-60) and the instant application are the same. Therefore, one must conclude that the diketopiperazines will complex the insulin incorporated in the microparticles of USPN '497 in the same manner as those described by Applicants' in the instant application.

The rejection on the ground of nonstatutory obviousness-type double patenting of claims 33 and 35-39 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4-7, and 10-12 of U.S. Patent No. 6,428,771 (USPN '771) **is maintained** for the reasons of record set forth on pages 10-11 of the office action mailed on May 17, 2006.

Response to Arguments

Applicant's arguments filed 10/9/07 have been fully considered but they are not persuasive. Applicants' traversal is based on their assertion that the claims of USPN '771 do not define microparticles wherein insulin is complexed with microparticles of a diketopiperazine. The Examiner respectfully disagrees. Applicants' arguments are the same as those discussed previously in the instant office action and the Examiner's position is the same as applied to the instant rejection. The microparticles of USPN '771 would obviously form complexes with

insulin, especially since the same microparticles are being used. It is noted that the chemical structure and description thereof used to define the diketopiperazines in the original specifications of USPN '771 (i.e. col. 4, lines 1-60) and the instant application are the same. Therefore, one must conclude that the diketopiperazines will complex the insulin incorporated in the microparticles of USPN '771 in the same manner as those described by Applicants' in the instant application.

The provisional rejections on the ground of nonstatutory obviousness-type double patenting of (1) claims 33, 35-39, and 42 as being unpatentable over claims 23-26 and 40-46 of copending Application No. 10/706,243 (copending '243); (2) claims 33-39 and 42 as being unpatentable over claims 1-5, 8-10, 16-17, 23-24, 26-30, and 36 of copending Application No. 11/210,710 (copending '710); and (3) claims 33-35 and 40-42 as being unpatentable over claims 1-5 and 17-23 of copending Application No. 11/329,686 (copending '686) **are maintained** for the reasons of record set forth on pages 12-15 of the office action mailed on May 17, 2006.

Response to Arguments

Applicant's arguments filed 10/9/07 have been fully considered but they are not persuasive. Applicants' arguments traversing (1) are not found persuasive, per the reasons of record and reiterated above in the instant office action that the claimed diketopiperazine microparticles of copending '243 do contain insulin complexed with said microparticles. Regarding (2)-(3), Applicants have asserted that these rejections should be withdrawn because

the instant application is allegedly in condition for allowance. The Examiner disagrees; the instant application is not in condition for allowance. These rejections are maintained.

Conclusion

Claims 33 and 35-42 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-6:30, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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